Drug Coverage Policy

Effective Date.....05/01/2026
Coverage Policy Number.....IP0182
Policy Title.....Spinraza

Spinal Muscular Atrophy – Spinraza

- Spinraza® (nusinersen intrathecal injection – Biogen)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview
Spinraza, a survival motor neuron 2 (SMN2)-directed antisense oligonucleotide, is indicated for the treatment of spinal muscular atrophy in pediatric and adult patients.[1]

Disease Overview
Spinal muscular atrophy is a genetic, autosomal recessive muscular disorder caused by deletion or loss of function mutation in the SMN1 gene.[2-5] The estimated incidence in the US is one in 11,000.[3] The reduced level of SMN protein causes degeneration of lower motor neurons.[2-5] The phenotypic expression of the disease is impacted by the SMN2 gene copy number. Data have shown that patients with a higher number of SMN2 copies generally have a more mild phenotypic disease expression. Gene deletion testing for spinal muscular atrophy can be performed at many diagnostic laboratories. Table 1 describes the disease types. Of note, various motor ability assessments are used in clinical practice to characterize functional impairment in spinal muscular atrophy. Different functional motor scales are utilized to evaluate patients. When motor neuron function is lost, it cannot be regained, which greatly impacts patients who have experienced progression (e.g., patients with complete paralysis of limbs or permanent ventilator dependence).

Table 1. Types of Spinal Muscular Atrophy.[4,5]

	Age at Onset	Features/Clinical Presentation/Motor Milestones*	Lifespan*	SMN2 Gene Copy Number
Type 0 (< 1% of patients)	Prenatal	Severe hypotonia and weakness with respiratory failure at birth. There is no achievement of motor milestones.	A few weeks to days [< 6 months]	1
Type 1 (50%)	< 6 months	Poor muscle tone and lack of movement. Respiratory assistance may be needed. Some head control. Patients are never able to sit without support.	< 2 years	1 to 2 for 80% of patients
Type 2 (30% of patients)	6 to 18 months	Patients are able to sit. However, patients are unable to walk or stand without assistance.	Close to normal	2 to 3 for over 90% of patients
Type 3 (10% to 20% of patients)	> 18 months	Walks independently but may lose this ability as the disease progresses. There is loss of motor skills.	Normal	3 to 5 for most patients
Type 4 (< 1% of patients)	> 18 years	Independent walking. Fatigue and proximal muscle weakness.	Normal	4 for 75% of patients; 5 or 6 for 25% of patients

* With supportive care only; SMN2 – Survival motor neuron 2.

Clinical Efficacy
Spinraza was investigated in a pivotal trial called ENDEAR, which was a Phase III, multicenter, multinational, randomized, double-blind, sham-procedure controlled study involving 121 symptomatic infants diagnosed with infantile-onset spinal muscular atrophy (Type 1).[1,6] Patients were randomized 2:1 to receive either Spinraza (n = 80) or sham injection (n = 41).[1] Eligible patients were ≤ 7 months of age at the time of the first dose and diagnosed with spinal muscular

atrophy with a symptom onset prior to 6 months of age. Baseline demographics were balanced between the Spinraza and control groups with the exception of age at first treatment (median age of 175 and 206 days, respectively).[1] At baseline, all infants were symptomatic, hypotonic and weak, which are features consistent with a phenotype that is most likely to be categorized as spinal muscular atrophy Type 1.[6] Patients had two SMN2 gene copies. The median time of treatment was 261 days (range 6 to 442 days).[1] Those who received Spinraza compared with sham-control experienced improvement on achieving motor milestone responses. Outcomes assessing survival also revealed improvements for patients receiving Spinraza vs. sham control.

CHERISH was a multicenter, double-blind, sham-controlled, Phase III trial which involved children with symptomatic later-onset spinal muscular atrophy who were 2 to 12 years of age (n = 126) with likely Type 2 or 3 disease (symptom onset after 6 months of age).[1,7] Patients were randomized (2:1) to receive Spinraza or sham injection. Three SMN2 gene copies were reported among 88% of patients; approximately 8% of patients had two SMN2 gene copies. The median age at screening was 4 years and 3 years in the Spinraza and sham procedure control groups, respectively.[1,7] Patients who received Spinraza experienced more improvement in motor milestones compared with sham control.

NURTURE was an open-label uncontrolled trial involving patients with presymptomatic spinal muscular atrophy who ranged in age from 3 days to 42 days at the time of the first dose (n = 25).[1,8] Patients were required to have two or three SMN2 gene copies.[8] Some patients who were given Spinraza prior to the onset of symptoms related to spinal muscular atrophy survived without requiring permanent ventilation beyond what would be anticipated based on their SMN2 copy number. Also, some patients also met age-appropriate growth and development motor milestones (e.g., ability to sit unassisted, stand, or walk). Data are available from almost a median of 3-year follow-up.

The EMBRACE trial showed benefits of Spinraza in infants/children with infantile- or later-onset spinal muscular atrophy who were not eligible for the ENDEAR or CHERISH studies.[9]

Dosing
Spinraza is given intrathecally by, or under the direction of, healthcare professionals experienced in performing lumbar punctures.[1] The recommended dosage is 12 mg (5 mL) per administration. Initiate Spinraza treatment with four loading doses. The first three loading doses should be administered at 14-day intervals. The fourth loading dose should be given 30 days after the third dose. A maintenance dose should be given once every 4 months thereafter. There are additional recommendations in patients who have missed doses.

Guidelines
The Spinal Muscular Atrophy Newborn Screening Multidisciplinary Working Group is comprised of clinicians and geneticists with expertise in spinal muscular atrophy who developed a treatment algorithm in 2018 for infants who have positive results from a newborn screening test for spinal muscular atrophy.[10] Spinal muscular atrophy Types 1 and 2 comprise a large majority of cases and account for many patients who screen positively for spinal muscular atrophy with three or fewer SMN2 gene copies. Immediate treatment is recommended in patients with two or three SMN2 gene copies. Treatment recommendations for patients who screen positive for spinal muscular atrophy and have only one SMN2 gene copy is more complicated.[10] In 2020, the Working Group updated recommendations that infants diagnosed with spinal muscular atrophy via newborn screening with four SMN2 gene copies should receive immediate treatment.[11] Also, patients with five (or more) SMN2 gene copies should be observed and screened for symptoms.

Coverage Policy

POLICY STATEMENT

Prior Authorization is required for benefit coverage of Spinraza. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Due to the specialized skills required for evaluation and diagnosis of patients treated with Spinraza as well as the monitoring required for adverse events and long-term efficacy, approval requires Spinraza to be prescribed by a physician who has consulted with or who specializes in the condition. If claims history is available, verification is required in certain criteria as noted by **[verification in claims history required]**. All reviews will be forwarded to the Medical Director for evaluation.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory results, medical test results, claims records, prescription receipts, and/or other information. All documentation must include patient-specific identifying information.

Spinraza is considered medically necessary when the following are met:

FDA-Approved Indication

1. **Spinal Muscular Atrophy (SMA) - Treatment.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A.** Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, iii, iv and v):
     - **i.** Baseline motor ability assessment that suggests spinal muscular atrophy (based on age, motor ability, and development) has been performed from **ONE** of the following exams (a, b, c, d, e, f, or g) **[documentation required]**:
       - **a.** Bayley Scales of Infant and Toddler Development; OR
       - **b.** Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND); OR
       - **c.** Hammersmith Functional Motor Scale Expanded (HFMSE); OR
       - **d.** Hammersmith Infant Neurological Exam Part 2 (HINE-2); OR
       - **e.** Motor Function Measure-32 Items (MFM-32); OR
       - **f.** Revised Upper Limb Module (RULM) Test; OR
       - **g.** World Health Organization motor milestone scale; AND
     - **ii.** Patient has a genetic test confirming the diagnosis of spinal muscular atrophy with bi-allelic pathogenic variants in the survival motor neuron 1 (SMN1) gene **[documentation required]**; AND
       Note: Pathogenic variants may include homozygous deletion, compound heterozygous mutation, or a variety of other rare mutations.
     - **iii.** Patient meets **ONE** of the following (a or b):
       - **a.** Patient has two or three survival motor neuron 2 (SMN2) gene copies **[documentation required]**; OR
       - **b.** Patient meets **BOTH** of the following ([1] and [2]):
         - **(1)** Patient has four survival motor neuron 2 (SMN2) gene copies **[documentation required]**; AND
         - **(2)** Patient has objective signs consistent with spinal muscular atrophy Types 1, 2, or 3 **[documentation required]**; AND

iv. Patient has not received Zolgensma (onasemnogene abeparvovec-xioi intravenous infusion) or Itvisma (onasemnogene abeparvovec-brve intrathecal injection) in the past **[verification in claims history required]**; AND
Note: If no claim for Zolgensma or Itvisma is present (or if claims history is not available), the prescribing physician confirms that the patient has not previously received Zolgensma or Itvisma.

v. The medication is prescribed by a physician who has consulted with or who specializes in the management of patients with spinal muscular atrophy and/or neuromuscular disorders; OR

B. Patient Currently Receiving Spinraza Therapy. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, iv, and v).

i. Patient has had a genetic test confirming the diagnosis of spinal muscular atrophy with bi-allelic pathogenic variants in the survival motor neuron 1 (SMN1) gene; AND
Note: Pathogenic variants may include homozygous deletion, compound heterozygous mutation, or a variety of other rare mutations.

ii. Patient meets ONE of the following (a or b):

a) Patient has two or three survival motor neuron 2 (SMN2) gene copies; OR

b) Patient meets BOTH of the following [(1) and (2)]:

(1) Patient has four survival motor neuron 2 (SMN2) gene copies; AND

(2) Patient has objective signs consistent with spinal muscular atrophy Types 1, 2, or 3; AND

iii. Each Spinraza dose is to be administered once every 4 months as maintenance therapy; AND

iv. Medication is prescribed by a physician who has consulted with or who specializes in the management of patients with spinal muscular atrophy and/or neuromuscular disorders; AND

v. Patient must meet ONE of the following (a or b):

a) Patient must have had a positive clinical response (for example, improvement or stabilization) from pretreatment baseline status (i.e., within the past 4 months) with Spinraza from ONE of the following [(1), (2), (3), (4), (5), (6), or (7)] **[documentation required]**:

(1) Bayley Scales of Infant and Toddler Development; OR

(2) Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND); OR

(3) Hammersmith Functional Motor Scale Expanded (HFMSE); OR

(4) Hammersmith Infant Neurological Exam Part 2 (HINE-2); OR

(5) Motor Function Measure-32 Items (MFM-32); OR

(6) Revised Upper Limb Module (RULM) test; OR

(7) World Health Organization motor milestone scale; OR

b) According to the prescribing physician, the patient has responded to Spinraza and continues to benefit from ongoing Spinraza therapy by the most recent (i.e., within the past 4 months) physician monitoring/assessment tools **[documentation required]**.
Note: Examples include pulmonary function tests showing improvement, bulbar function test results suggest benefits, reduced need for respiratory support, decrease in the frequency of respiratory infections or complications, and/or prevention of permanent assisted ventilation.

Dosing. Approve the following dosing regimens:

- **A)** Initially, give 12 mg intrathecally as four loading doses of which the first three loading doses should be given at 14-day intervals and the fourth loading dose should be given 30 days after the third dose; AND/OR
- **B)** The maintenance dose is 12 mg intrathecally once every 4 months; AND/OR
- **C)** Missed maintenance doses must meet ONE of the following (i, ii, or iii):
  - **i.** At least 8 months but less than 16 months from the last dose: approve one 12 mg intrathecal dose to be given as soon as possible, followed by one additional dose 14 days later; OR
    Note: Thereafter, the regular maintenance dose schedule should be followed.
  - **ii.** At least 16 months but less than 40 months from the last dose: approve the 12 mg intrathecal maintenance dose to be given as soon as possible, followed by two additional doses that must be given 14 days apart; OR
    Note: Thereafter, the regular maintenance dose schedule should be followed.
  - **iii.** At least 40 months from the last dose. Dosing should be restarted as recommended in criterion A and B.

Conditions Not Covered

Spinraza for any other use is considered not medically necessary including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Patient has Complete Paralysis of All Limbs.** Data are needed to determine if this patient population with advanced spinal muscular atrophy would derive benefits from Spinraza.

2. **Patient has Permanent Ventilator Dependence.** Data are needed to determine if this patient population with advanced spinal muscular atrophy would derive benefits from Spinraza.

3. **Concurrent use of Evrysdi (risdiplam oral solution and tablets).** Further study is needed to determine if use of Spinraza with Evrysdi is efficacious and safe.

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J2326	Injection, nusinersen, 0.1 mg

References

1. Spinraza® intrathecal injection [prescribing information]. Cambridge, MA: Biogen; April 2024.

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3. Yeo CJJ, Tizzano EF, Darras BT. Challenges and opportunities in spinal muscular atrophy therapeutics. *Lancet Neurol*. 2024;23:205-218.
4. Ramdas S, Oskoui M, Servais L. Treatment options in spinal muscular atrophy: a pragmatic approach for clinicians. *Drugs*. 2024;84:747-762.
5. Prior TW, Leach ME, Finanger E. Spinal Muscular Atrophy. 2000 Feb 24 [Updated 2024 September 19]. In: Adam MP, Feldman J, Mirzaa GM, et al, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1352/pdf/Bookshelf_NBK1352.pdf. Accessed on July 26, 2025.
6. Finkel RS, Mercuri E, Darras BT, et al, for the ENDEAR Group. Nusinersen versus sham control in infantile-onset spinal muscular atrophy. *N Engl J Med*. 2017;377(18):1723-1732.
7. Mercuri E, Darras BT, Chiriboga JW, et al, for the CHERISH Study Group. Nusinersen versus sham control in later-onset spinal muscular atrophy. *N Engl J Med*. 2018;378:625-635.
8. De Vivo DC, Bertini E, Swoboda KJ, et al. Nusinersen initiated in infants during the presymptomatic stage of spinal muscular atrophy: interim efficacy and safety results from the Phase 2 NURTURE study. *Neuromuscular Dis*. 2019;29:842-856.
9. Acsadi G, Crawford TO, Muller-Felber W, et al. Safety and efficacy of nusinersen in spinal muscular atrophy: the EMBRACE study. *Muscle Nerve*. 2021;63:668-677.
10. Glascock J, Sampson J, Haidet-Phillips A, et al. Treatment algorithm for infants diagnosed with spinal muscular atrophy through newborn screening. *J Neuromuscul Dis*. 2018;5:145-158.
11. Glascock J, Sampson J, Connolly AM, et al. Revised recommendations for the treatment of infants diagnosed with spinal muscular atrophy via newborn screening who have 4 copies of SMN2. *J Neuromuscul Dis*. 2020;7(2):97-100.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	No criteria changes	12/15/2024
Annual Revision	**Policy Title:** From "Nusinersen" to "Spinal Muscular Atrophy – Spinraza". **Spinal Muscular Atrophy – Treatment:** **Updated** documentation requirements throughout the policy. For Initial Therapy **–** **Updated** the initial authorization duration from "6 months" to "3 months". **Removed** criterion requiring the "onset of clinical signs and symptoms consistent with SMA occur at age 15 years or younger". **Removed** the 6 Minute Walk Test from the list of baseline motor ability assessment options. **Updated** the genetic testing language from "Bi-allelic mutation" to "bi-allelic pathogenic variants". **Added** "patient has not received	08/15/2025

	Zolgensma". **Removed** follow-on Spinraza criteria in those who were previously treated with Zolgensma. For Patient Currently Receiving **-** **Updated** the reauthorization duration from "12 months" to "4 months". **Added** criteria for a patient currently receiving Spinraza. **Conditions Not Covered:** **Updated** the Conditions Not Covered statement. **Updated** "Concurrent use of Evrysdi" statement.	
Selected Revision	**Spinal Muscular Atrophy – Treatment:** For initial therapy, Itvisma was added as a gene therapy that the patient should not have received in the past. The Note now includes that if no claim for Itvisma is present (or if claims history is not available), the prescribing physician confirms that the patient has not previously received Itvisma. Missed maintenance doses for at least 8 months but less than 16 months was corrected to say, followed by one additional dose 14 days later, previously it stated two doses. For Patients Currently Receiving Spinraza Therapy, Approval duration was updated to 1 year, previously it was one dose to be used once within the next 4 months as maintenance therapy. **Coding Information** **Removed** CPT code 96450	3/15/2026
Selected Revision	**Spinal Muscular Atrophy – Treatment:** The requirement that 4 months has elapsed since the last dose was changed to each Spinraza dose is to be administered once every 4 months as maintenance therapy.	5/1/2026

The policy effective date is in force until updated or retired.